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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/810,733	03/26/2004	Qiong Cheng	CL2385USNA	3038

23906 7590 11/15/2006

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EXAMINER
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LEE, JAE W

ART UNIT	PAPER NUMBER
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1656

DATE MAILED: 11/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/810,733

Applicant(s)

CHENG ET AL.

Examiner

Jae W. Lee

Art Unit

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 09/07/2006
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 15, 17-19, 36 and 37 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 36 is/are allowed.
- 6) ☒ Claim(s) 15, 17-19 and 37 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application
- ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Application status***

Applicants' amendment to claims 6 (cancelled), 18 (amended) and 19 (amended), and the addition of new claims 36 and 37, filed on 09/07/2006, is acknowledged. Applicants' arguments, filed on 09/07/2006, are acknowledged. Claims 15, 17-19, 36 and 37 are at issue and present for examination. Applicants' arguments filed on 09/07/2006, have been fully considered, and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### ***Election/Restrictions***

Applicants' traversed the restriction requirement for claims 4, 5, and 20-35. However, claims 4, and 5 are drawn to a polypeptide, classified in class 435, subclass 183; claims 20-27 are drawn to a method of producing carotenoid compounds, classified in class 435, subclass 67; claims 28-32 are drawn to a method of regulating carotenoid biosynthesis in an organism, classified in class 435, subclass 471; claim 33 is drawn to a strain DC413, classified in class 435, subclass 252.3; and claim 34 is drawn to all isolated nucleic acid molecule encoding all of the amino acid sequences as set forth in SEQ ID NO: 2, 4, 6, 8, 10, 12, and 14, classified in class 536, subclass 23.1. Because these inventions are classified differently and they are patentably distinct for the reasons stated in the non-final rejection, filed on 08/30/2006, Applicants' arguments

is found non-persuasive and the restriction requirement is deemed proper under 35 U.S.C. 121.

### ***Claim Objections***

Claim 35 is objected to because it depends from a non-existent claim.

Claims 15 and 17-19 are objected to because they depend from the cancelled claim 6, which is necessitated by the Applicants' amendment, filed on 09/07/2006.

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15, 17-19 and 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule of SEQ ID NO: 20 encoding all of the following enzymes a) geranylgeranyl pyrophosphate synthetase of SEQ ID NO: 2; b) zeaxanthine glucosyl transferase of SEQ ID NO: 4; c) lycopene cyclase of SEQ ID NO: 6; d) phytoene desaturase of SEQ ID NO: 8; e) phytoene synthase of SEQ ID NO: 10; f)  $\beta$ -carotene hydroxylase of SEQ ID NO: 12; and g) isopentenyl diphosphate isomerase of SEQ ID NO: 14., does not reasonably provide enablement for any isolated nucleic acid having 95% identity to SEQ ID NO 20 and

encoding all of the following enzymes (a)-(g). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claim 37 is so broad as to encompass any nucleic acid having 95% sequence identity to SEQ ID NO 20 encoding all of the following enzymes a) any geranylgeranyl pyrophosphate synthetase; b) any zeaxanthine glucosyl transferase; c) any lycopene cyclase; d) any phytoene desaturase; e) any phytoene synthase; f) any  $\beta$ -carotene hydroxylase; and g) any isopentenyl diphosphate isomerase (see above 112 2<sup>nd</sup> paragraph rejection). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acids broadly encompassed by the claims, encoding the polypeptides, a) geranylgeranyl pyrophosphate synthetase; b) zeaxanthine glucosyl transferase; c) lycopene cyclase; d) phytoene desaturase; e) phytoene synthase; f)  $\beta$ -carotene hydroxylase; and g) isopentenyl diphosphate isomerase, by any nucleic acid having 95% identity to SEQ ID NO 20. The claims rejected under this section of U.S.C. 112,

Art Unit: 1656

first paragraph, place no structure/function limitations on the claimed nucleic acids.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and thus nucleic acid sequence while obtaining the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications among any of the 9127 nucleic acid residues or any 456 nucleic acid residues of SEQ ID NO: 20 (5 % of the SEQ ID NO: 20), as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

It is noted that claims 15 and 17-19 continue to be rejected to the extent that it is Applicants' intent that they depend from claim 37, which was newly added for the purpose of replacing claim 6, as disclosed in the Applicants' argument on pg. 9, line 1-2, filed on 09/07/2006. Thus, said claims are continued to be rejected because they improperly depend from the cancelled claim 6.

Art Unit: 1656

of preferred codons for specific host cell expression) may be made to such a gene cluster without affecting its utility provided that all of the encoded polypeptides are expressed and are enzymatically active. Applicants have not provided guidance to make a majority of the encompassed isolated nucleic acid molecule having at least 95% identity to SEQ ID NO 20, wherein said nucleic acid molecule encodes all of the enzymes a) geranylgeranyl pyrophosphate synthetase; b) zeaxanthine glucosyl transferase; c) lycopene cyclase; d) phytoene desaturase; e) phytoene synthase; f)  $\beta$ -carotene hydroxylase; and g) isopentenyl diphosphate isomerase. The specification does not support the broad scope of the claims because the specification does not establish: (A) regions of the nucleic acid structure which may be modified without affecting the encoded proteins' functions/activities; (B) the general tolerance of the protein to modification and the extent of such tolerance; (C) a rational and predictable scheme for modifying SEQ ID NO: 20 thereby changing amino acid residue of the encoded polypeptides with an expectation of obtaining the desired biological function; and (D) the insufficient guidance in the specification as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions at which location among as many as 456 nucleotides (5% of the SEQ ID NO 20), would be acceptable to retain the desired polypeptide functions/activities and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser,

Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those nucleic acid molecules.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any isolated nucleic acid molecule having at least 95% sequence identity to SEQ ID NO 20 and encoding all of the following enzymes: a) geranylgeranyl pyrophosphate synthetase; b) zeaxanthine glucosyl transferase; c) lycopene cyclase; d) phytoene desaturase; e) phytoene synthase; f)  $\beta$ -carotene hydroxylase; and g) isopentenyl diphosphate isomerase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those nucleic acids having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Although, Applicants argue that the number of nucleic acid molecules that encode all the recited polypeptide having 95% identity to SEQ ID NO: 20 is very small while retaining the enzymatic function of each protein, a skilled artisan would not recognize which 456 nucleotides out of 9127 would can be substituted, modified or changed and still maintain desired level of enzymatic activity for each protein.



Art Unit: 1656

Therefore, there is still insufficient guidance to practice the invention with respect to this issue.

Further, it is noted that Applicants have amended claim 18 in response to a rejection under this statute for the inclusion of green plants. However, claims 17-19 still encompass a transformed host from green plants. Previous studies demonstrate that the transformation of plants or the gene transfer to plants have been difficult with low success rate (Potrykus, Biotechnology 8(6): 535-542). In this regard, the specification fails to disclose a representative example of a successful transformation of a green plant host with the nucleic acid molecule of SEQ ID NO 20. Thus, Applicants have not provided sufficient guidance to make such.

#### ***Remarks***

Claims 15, 17-19 and 37 are not allowed.

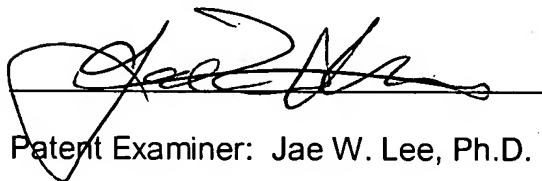
#### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jae W. Lee whose telephone number is 571-272-9949. The examiner can normally be reached on 8:30 am - 5:00 pm.

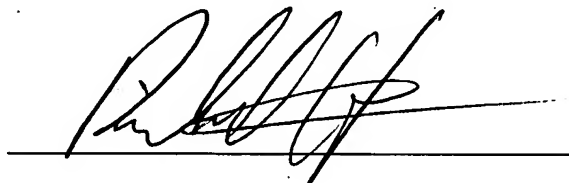
If attempts to reach the examiner by telephone are unsuccessful, please contact the examiner's supervisor, Kathleen Kerr at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-9949.

Art Unit: 1656

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Patent Examiner: Jae W. Lee, Ph.D.



**RICHARD HUTSON, PH.D.  
PRIMARY EXAMINER**